APPLICATION FOR UNITED STATES PATENT IN THE NAME

Of

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For

METHODS OF COATING AN IMPLANTABLE DEVICE

DOCKET NO. 50623.00041 (2742)

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METHODS OF COATING AN IMPLANTABLE DEVICE

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CROSS-REFERENCE

[0001] This is a continuation-in-part of application serial number 09/844,522, which was filed on April 27, 2001.

BACKGROUND OF THE INVENTION

Field of the Invention

[0002] This invention relates to methods of coating an implantable device, such as a stent.

Description of the Background

[0003] Blood vessel occlusions are commonly treated by mechanically enhancing blood flow in the affected vessels, such as by employing a stent. Stents act as scaffoldings, functioning to physically hold open and, if desired, to expand the wall of the passageway. Typically stents are capable of being compressed, so that they can be inserted through small lumens via catheters, and then expanded to a larger diameter once they are at the desired location. Examples in the patent literature disclosing stents include U.S. Patent No. 4,733,665 issued to Palmaz, U.S. Patent No. 4,800,882 issued to Gianturco, and U.S. Patent No. 4,886,062 issued to Wiktor.

[0004] Figure 1 illustrates a conventional stent 10 formed from a plurality of struts 12. The plurality of struts 12 are radially expandable and interconnected by connecting elements 14 that are disposed between adjacent struts 12, leaving lateral openings or gaps 16 between adjacent struts 12. Struts 12 and connecting elements 14 define a tubular stent body having an outer, tissue-contacting surface and an inner surface.

[0005] Stents are used not only for mechanical intervention but also as vehicles for providing biological therapy. Biological therapy can be achieved by medicating the stents. Medicated stents provide for the local administration of a therapeutic substance at the diseased site. Local delivery of a therapeutic substance is a preferred method of treatment because the substance is concentrated at a specific site and thus smaller total levels of medication can be administered in comparison to systemic dosages that often produce adverse or even toxic side effects for the patient.

[0006] One method of medicating a stent involves the use of a polymeric carrier coated onto the surface of the stent. A composition including a solvent, a polymer dissolved in the solvent, and a therapeutic substance dispersed in the blend is applied to the stent by immersing the stent in the composition or by spraying the composition onto the stent. The solvent is allowed to evaporate, leaving on the stent strut surfaces a coating of the polymer and the therapeutic substance impregnated in the polymer.

[0007] A shortcoming of the above-described method of medicating a stent is the potential for coating defects due to the large amount of liquid composition applied to

the relatively small surface area of the stent. The liquid composition can flow, wick, and collect as the amount of composition on the stent increases during the coating process. As the solvent evaporates, the excess composition hardens, leaving the excess coating as clumps or pools on the struts or webbing between the struts.

[0008] Another shortcoming of the above-described method of medicating a stent is the potential for loss of the therapeutic substance from the coating or production of a coating that does not provide for a suitable residence time of the substance at the implanted region. Initial portions of a liquid composition containing a therapeutic substance sprayed onto a stent adhere to the stent surface. However, as the liquid composition continues to be applied to the stent, layers of the composition are formed on top of one another. When exposed to the solvent in the upper layers, the therapeutic substance in the lower layers can be re-dissolved into the upper layers of the composition or extracted out from the coating. Having the therapeutic substance maintained in merely the upper regions of the coating provides for a short residence time of the substance at the implanted region, as the therapeutic substance will be quickly released. Prolonged residence times *in situ* may be desirable for a more effective treatment of a patient.

[0009] The present invention addresses such problems by providing methods of coating implantable devices.

SUMMARY OF THE INVENTION

[0010] The present invention provides a method of coating an implantable device, such as a stent. The method includes adjusting the temperature of the implantable device to a temperature other than ambient temperature and applying a coating substance to the implantable device.

[0011] In one embodiment, adjusting includes increasing the temperature of the implantable device. In another embodiment, the implantable device is a metallic stent.

[0012] The present invention also provides another method of coating an implantable device. The method includes applying a composition including a fluid to an implantable device and directing a gas onto the implantable device to induce evaporation of the fluid from the composition to form a coating on the implantable device. The acts of applying and directing can be repeated to form a coating of a desirable thickness or weight.

[0013] In some embodiments, the act of applying includes spraying the composition onto the implantable device. Such spraying can be performed at a flow rate of about 0.1 mg/sec to about 1 mg/sec and for a duration of about 0.5 seconds to about 5 seconds.

[0014] In some embodiments, the temperature of the gas is about 25°C to about 200°C, at a flow speed of about 0.01 m^3/second to about 1.42 m^3/second, and for a duration of about 1 second to about 100 seconds.

[0015] In one embodiment, the method can additionally include rotating the implantable device about the longitudinal axis of the implantable device. In another embodiment, the method can additionally include moving the implantable device in a linear direction along the longitudinal axis of the implantable device.

[0016] Also provided is a method of coating a stent. The method includes spraying onto a stent a composition including a solvent, a polymer dissolved in the solvent, and optionally an active agent. The method also includes applying a warm gas onto the stent to remove the solvent from the composition and form a coating on the stent. The acts of spraying and applying can be repeated to form a coating of a desirable thickness or weight.

BRIEF DESCRIPTION OF THE FIGURES

[0017] Figure 1 illustrates a conventional stent.

DETAILED DESCRIPTION

[0018] For ease of discussion, the methods detailed herein will be described with reference to coating a stent. However, the device or prosthesis coated in accordance with embodiments of the present invention may be any suitable medical substrate that can be implanted in a human or veterinary patient. Examples of such implantable devices include self-expandable stents, balloon-expandable stents, stent-grafts, grafts (e.g., aortic grafts), artificial heart valves, cerebrospinal fluid shunts, pacemaker electrodes, and endocardial leads (e.g., FINELINE and ENDOTAK, available from

Guidant Corporation). The underlying structure of the device can be of virtually any design. The device can be made of a metallic material or an alloy such as, but not limited to, cobalt chromium alloy (ELGILOY), stainless steel (316L), high nitrogen stainless steel, e.g., BIODUR 108, cobalt chrome alloy L-605, "MP35N," "MP20N," ELASTINITE (Nitinol), tantalum, nickel-titanium alloy, platinum-iridium alloy, gold, magnesium, or combinations thereof. "MP35N" and "MP20N" are trade names for alloys of cobalt, nickel, chromium and molybdenum available from Standard Press Steel Co., Jenkintown, PA. "MP35N" consists of 35% cobalt, 35% nickel, 20% chromium, and 10% molybdenum. "MP20N" consists of 50% cobalt, 20% nickel, 20% chromium, and 10% molybdenum. Devices made from bioabsorbable or biostable polymers could also be used with the embodiments of the present invention.

<u>Coating A Stent</u>

[0019] To form a coating on a stent, a composition is sprayed onto the stent. A spray apparatus, such as EFD 780S spray device with VALVEMATE 7040 control system (manufactured by EFD Inc., East Providence, RI), can be used to apply the composition to the stent. EFD 780S spray device is an air-assisted external mixing atomizer. The composition is atomized into small droplets by air and uniformly applied to the stent surfaces. The atomization pressure can be maintained at a range of about 5 psi to about 20 psi. The droplet size depends on factors such as viscosity of the solution, surface tension of the solvent, and atomization pressure. Other types of

spray applicators, including air-assisted internal mixing atomizers and ultrasonic applicators, can also be used for the application of the composition.

[0020] During the application of the composition, the stent can be rotated about the stent's central longitudinal axis. Rotation of the stent can be from about 0.1 rpm to about 300 rpm, more narrowly from about 1 rpm to about 10 rpm. By way of example, the stent can rotate at about 3 rpm. The stent can also be moved in a linear direction along the same axis. The stent can be moved at about 1 mm/second to about 12 mm/second, for example about 6 mm/second, or for a minimum of at least two passes (i.e., back and forth past the spray nozzle).

[0021] The flow rate of the composition from the spray nozzle can be from about 0.01 mg/second to about 1.0 mg/second, more narrowly about 0.1 mg/second. Only a small percentage of the composition that is delivered from the spray nozzle is ultimately deposited on the stent. By way of example, when a composition is sprayed to deliver about 1 mg of solids, only about 100 micrograms or about 10% of the solids sprayed will likely be deposited on the stent. Multiple repetitions for applying the composition can be performed, wherein each repetition can be, for example, about 0.5 second to about 5 seconds in duration. The amount of coating applied by each repetition can be about 1 microgram/cm^2 (of stent surface) to about 50 micrograms/cm^2, for example less than about 20 micrograms/cm^2 per 1-second spray.

[0022] Each repetition can be followed by removal of a significant amount of the solvent(s). The removal of the solvent(s) can be performed following a waiting period

of about 0.1 second to about 5 seconds after the application of the coating composition so as to allow the liquid sufficient time to flow and spread over the stent surface before the solvent(s) is removed to form a coating. The waiting period is particularly suitable if the coating composition contains a volatile solvent, such as solvents having boiling points >130°C at ambient pressure, since such solvents are typically removed quickly.

[0023] Removal of the solvent(s) can be induced by the application of a warm gas. The application of a warm gas between each repetition prevents coating defects and minimizes interaction between the active agent and the solvent. Any suitable gas can be employed, examples of which include air or nitrogen. The temperature of the warm gas can be from about 25°C to about 200°C, more narrowly from about 40°C to about 90°C. The flow speed of the gas can be from about 0.5 $feet^3$/second (0.01 $meters^3$/second) to about 50 $feet^3$/second (1.42 $meters^3$/second), more narrowly about 2.5 $feet^3$/second (0.07 $meters^3$/second) to about 15 $feet^3$/second (0.43 $meters^3$/second). The gas can be applied for about 1 second to about 100 seconds, more narrowly for about 2 seconds to about 20 seconds. By way of example, warm gas applications can be performed at a temperature of about 60°C, at a flow speed of about 10 $feet^3$/second, and for about 10 seconds.

[0024] In one embodiment, the stent can be warmed to a temperature of from about 35°C to about 80°C prior to the application of the coating composition so as to facilitate faster removal of the solvent(s). The particular temperature selected

depends, at least in part, on the particular active agent employed in the coating composition. By way of example, pre-heating of the stent prior to applying a composition containing actinomycin D should be performed at a temperature not greater than about 55°C. Pre-heating is particularly suitable for embodiments in which the solvent(s) employed in the coating composition has a high boiling point, i.e., volatile solvents having boiling points of, for example, >130°C at ambient pressure (e.g., dimethylsulfoxide (DMSO), dimethylformamide (DMF), and dimethylacetamide (DMAC)).

[0025] Any suitable number of repetitions of applying the composition followed by removing the solvent(s) can be performed to form a coating of a desired thickness or weight. Excessive application of the polymer can, however, cause coating defects. In embodiments in which the coating composition contains a volatile solvent, a waiting period of from about 0.1 second to about 20 seconds can be employed between solvent removal of one repetition and composition application of the subsequent repetition so as to ensure that the wetting rate of the coating composition is slower than the evaporation rate of the solvent within the composition, thereby promoting coating uniformity.

[0026] Operations such as wiping, centrifugation, or other web clearing acts can also be performed to achieve a more uniform coating. Briefly, wiping refers to the physical removal of excess coating from the surface of the stent; and centrifugation

refers to rapid rotation of the stent about an axis of rotation. The excess coating can also be vacuumed off of the surface of the stent.

[0027] In accordance with one embodiment, the stent can be at least partially pre-expanded prior to the application of the composition. For example, the stent can be radially expanded about 20% to about 60%, more narrowly about 27% to about 55% -- the measurement being taken from the stent's inner diameter at an expanded position as compared to the inner diameter at the unexpanded position. The expansion of the stent, for increasing the interspace between the stent struts during the application of the composition, can further prevent "cob web" formation between the stent struts.

[0028] A final heat treatment can be conducted to remove essentially all of the solvent(s) from the composition on the stent. The heat treatment can be conducted at about 30° C to about 200°C for about 15 minutes to about 16 hours, more narrowly at about 50°C to about 100°C for about 1 hour to about 4 hours. By way of example, the heat treatment can be conducted at about 75°C for 1 hour. The temperature of exposure should not adversely affect the characteristics of the active agent or of the coating. The heating can be conducted in an anhydrous atmosphere and at ambient pressure. The heating can, alternatively, be conducted under a vacuum condition. It is understood that essentially all of the solvent(s) will be removed from the composition but traces or residues can remain blended in the coating.

[0029] By way of example, and not limitation, the coating, referred to herein as the primary or reservoir coating, can have a thickness of about 0.05 microns to about 10 microns. The particular thickness of the coating is based on the type of procedure for which the stent is employed and the amount, if any, of active agent that is desired to be delivered. Applying a plurality of reservoir coating layers, containing the same or different active agents, onto the stent can further increase the amount of the active ingredient to be carried by the stent, without causing coating defects.

Embodiments of the Composition

[0030] In accordance with one embodiment, the composition can include a solvent and a polymer dissolved in the solvent. The composition can also include active agents, radiopaque elements, or radioactive isotopes. Representative examples of polymers that can be used to coat a stent include ethylene vinyl alcohol copolymer (commonly known by the generic name EVOH or by the trade name EVAL), poly(hydroxyvalerate); poly(L-lactic acid); polycaprolactone; poly(lactide-co-glycolide); poly(hydroxybutyrate); poly(hydroxybutyrate-co-valerate); polydioxanone; polyorthoester; polyanhydride; poly(glycolic acid); poly(D,L-lactic acid); poly(glycolic acid-co-trimethylene carbonate); polyphosphoester; polyphosphoester urethane; poly(amino acids); cyanoacrylates; poly(trimethylene carbonate); poly(iminocarbonate); copoly(ether-esters) (e.g. PEO/PLA); polyalkylene oxalates; polyphosphazenes; biomolecules, such as fibrin, fibrinogen, cellulose, starch, collagen and hyaluronic acid; polyurethanes; silicones; polyesters; polyolefins; polyisobutylene

and ethylene-alphaolefin copolymers; acrylic polymers and copolymers; vinyl halide polymers and copolymers, such as polyvinyl chloride; polyvinyl ethers, such as polyvinyl methyl ether; polyvinylidene halides, such as polyvinylidene fluoride and polyvinylidene chloride; polyacrylonitrile; polyvinyl ketones; polyvinyl aromatics, such as polystyrene; polyvinyl esters, such as polyvinyl acetate; copolymers of vinyl monomers with each other and olefins, such as ethylene-methyl methacrylate copolymers, acrylonitrile-styrene copolymers, ABS resins, and ethylene-vinyl acetate copolymers; polyamides, such as Nylon 66 and polycaprolactam; alkyd resins; polycarbonates; polyoxymethylenes; polyimides; polyethers; epoxy resins; polyurethanes; rayon; rayon-triacetate; cellulose; cellulose acetate; cellulose butyrate; cellulose acetate butyrate; cellophane; cellulose nitrate; cellulose propionate; cellulose ethers; and carboxymethyl cellulose.

[0031] "Solvent" is defined as a liquid substance or composition that is compatible with the polymer and is capable of dissolving the polymer at the concentration desired in the composition. Examples of solvents include, but are not limited to, dimethylsulfoxide (DMSO), chloroform, acetone, water (buffered saline), xylene, methanol, ethanol, 1-propanol, tetrahydrofuran, 1-butanone, dimethylformamide, dimethylacetamide, cyclohexanone, ethyl acetate, methylethylketone, propylene glycol monomethylether, isopropanol, isopropanol admixed with water, N-methyl pyrrolidinone, toluene, and combinations thereof.

[0032] The active agent can be for inhibiting the activity of vascular smooth muscle cells. More specifically, the active agent can be aimed at inhibiting abnormal or inappropriate migration and/or proliferation of smooth muscle cells for the inhibition of restenosis. The active agent can also include any substance capable of exerting a therapeutic or prophylactic effect in the practice of the present invention. For example, the agent can be for enhancing wound healing in a vascular site or improving the structural and elastic properties of the vascular site. Examples of agents include antiproliferative substances such as actinomycin D, or derivatives and analogs thereof (manufactured by Sigma-Aldrich 1001 West Saint Paul Avenue, Milwaukee, WI 53233; or COSMEGEN available from Merck). Synonyms of actinomycin D include dactinomycin, actinomycin IV, actinomycin I_1, actinomycin X_1, and actinomycin C_1. The active agent can also fall under the genus of antineoplastic, antiinflammatory, antiplatelet, anticoagulant, antifibrin, antithrombin, antimitotic, antibiotic, antiallergic and antioxidant substances. Examples of such antineoplastics and/or antimitotics include paclitaxel (e.g. TAXOL® by Bristol-Myers Squibb Co., Stamford, Conn.), docetaxel (e.g. Taxotere®, from Aventis S.A., Frankfurt, Germany) methotrexate, azathioprine, vincristine, vinblastine, fluorouracil, doxorubicin hydrochloride (e.g. Adriamycin® from Pharmacia & Upjohn, Peapack N.J.), and mitomycin (e.g. Mutamycin® from Bristol-Myers Squibb Co., Stamford, Conn.). Examples of such antiplatelets, anticoagulants, antifibrin, and antithrombins include sodium heparin, low molecular weight heparins, heparinoids, hirudin, argatroban, forskolin, vapiprost, prostacyclin and prostacyclin analogues, dextran, D-phe-pro-arg-chloromethylketone

(synthetic antithrombin), dipyridamole, glycoprotein IIb/IIIa platelet membrane receptor antagonist antibody, recombinant hirudin, and thrombin inhibitors such as Angiomax ™ (Biogen, Inc., Cambridge, Mass.). Examples of such cytostatic or antiproliferative agents include angiopeptin, angiotensin converting enzyme inhibitors such as captopril (e.g. Capoten® and Capozide® from Bristol-Myers Squibb Co., Stamford, Conn.), cilazapril or lisinopril (e.g. Prinivil® and Prinzide® from Merck & Co., Inc., Whitehouse Station, NJ); calcium channel blockers (such as nifedipine), colchicine, fibroblast growth factor (FGF) antagonists, fish oil (omega 3-fatty acid), histamine antagonists, lovastatin (an inhibitor of HMG-CoA reductase, a cholesterol lowering drug, brand name Mevacor® from Merck & Co., Inc., Whitehouse Station, NJ), monoclonal antibodies (such as those specific for Platelet-Derived Growth Factor (PDGF) receptors), nitroprusside, phosphodiesterase inhibitors, prostaglandin inhibitors, suramin, serotonin blockers, steroids, thioprotease inhibitors, triazolopyrimidine (a PDGF antagonist), and nitric oxide. An example of an antiallergic agent is permirolast potassium. Other therapeutic substances or agents which may be appropriate include alpha-interferon, genetically engineered epithelial cells, rapamycin and dexamethasone. Exposure of the active ingredient to the composition should not adversely alter the active ingredient's composition or characteristic. Accordingly, the particular active ingredient is selected for compatibility with the solvent or blended polymer-solvent.

[0033] Examples of radiopaque elements include, but are not limited to, gold, tantalum, and platinum. An example of a radioactive isotope is P^{32}. Sufficient

amounts of such substances may be dispersed in the composition such that the substances are not present in the composition as agglomerates or flocs.

Optional Coating Layers

[0034] In one embodiment, an optional primer layer can be formed prior to the primary or reservoir coating to increase the retention of the primary or reservoir coating on the surface of the stent, particularly metallic surfaces such as stainless steel. The primer layer can act as an intermediary adhesive tie layer between the surface of the device and a reservoir coating carrying an active agent, allowing for the quantity of the active agent to be increased in the reservoir coating.

[0035] To form an optional primer layer on the surface of the stent, an embodiment of the above-described composition that is free from active agents is applied to the surface of the stent. Ethylene vinyl alcohol copolymer, for example, adheres very well to metallic surfaces, particularly stainless steel. Accordingly, the copolymer provides for a strong adhesive tie between the reservoir coating and the surface of the stent. With the use of thermoplastic polymers such as, but not limited to, ethylene vinyl alcohol copolymer, polycaprolactone, poly(lactide-co-glycolide), and poly(hydroxybutyrate), the deposited primer composition should be exposed to a heat treatment at a temperature range greater than about the glass transition temperature (T_g) and less than about the melting temperature (T_m) of the selected polymer. Unexpected results have been discovered with treatment of the composition under this temperature range, specifically strong adhesion or bonding of the coating to the

metallic surface of the stent. The prosthesis should be exposed to the heat treatment for any suitable duration of time that will allow for the formation of the primer layer on the surface of the stent and for the evaporation of the solvent employed. By way of example and not limitation, the optional primer layer can have a thickness of about 0.01 microns to about 2 microns. The application of the primary or reservoir coating should be performed subsequent to the drying of the optional primer layer.

[0036] In another embodiment, an optional diffusion barrier can be formed over a reservoir coating containing an active agent to help control the rate at which the active agent is released from the coated stent. An embodiment of the composition, free from any active agents, can be applied to a selected portion of the primary or reservoir coating subsequent to the drying of the reservoir coating. Application of the composition and evaporation of the solvent to form the diffusion barrier can be accomplished via embodiments of the above-described method of the present invention. The diffusion barrier can have a thickness of about 0.2 microns to about 10 microns. It is understood by one of ordinary skill in the art that the thickness of the diffusion barrier is based on factors such as the type of stent, the type of procedure for which the stent is employed, and the rate of release that is desired. As described above with reference to the primary or reservoir coating, a final heat treatment can be conducted to remove essentially all of the solvent(s) from the optional diffusion barrier.

Method of Use

[0037] In accordance with embodiments of the above-described method, an active agent can be applied to an implantable device or prosthesis, e.g., a stent, retained on the stent during delivery and expansion of the stent, and released at a desired control rate and for a predetermined duration of time at the site of implantation. The release rate of the active agent can be controlled by the addition of a diffusion barrier layer. A stent having the above-described coating is useful for a variety of medical procedures, including, by way of example, treatment of obstructions caused by tumors in bile ducts, esophagus, trachea/bronchi and other biological passageways. A stent having the above-described coating is particularly useful for treating occluded regions of blood vessels caused by abnormal or inappropriate migration and proliferation of smooth muscle cells, thrombosis, and restenosis. Stents may be placed in a wide array of blood vessels, both arteries and veins. Representative examples of sites include the iliac, renal, and coronary arteries.

[0038] Briefly, an angiogram is first performed to determine the appropriate positioning for stent therapy. An angiogram is typically accomplished by injecting a radiopaque contrasting agent through a catheter inserted into an artery or vein as an x-ray is taken. A guidewire is then advanced through the lesion or proposed site of treatment. Over the guidewire is passed a delivery catheter which allows a stent in its collapsed configuration to be inserted into the passageway. The delivery catheter is inserted either percutaneously or by surgery into the femoral artery, brachial artery,

femoral vein, or brachial vein, and advanced into the appropriate blood vessel by steering the catheter through the vascular system under fluoroscopic guidance. A stent having the above-described coating may then be expanded at the desired area of treatment. A post-insertion angiogram may also be utilized to confirm appropriate positioning.

EXAMPLES

[0039] The embodiments of the present invention will be illustrated by the following set forth examples, which are being given by way of illustration only and not by way of limitation. All parameters and data are not to be construed to unduly limit the scope of the embodiments of the invention.

Example 1

[0040] Four 8 mm Multi-Link TETRA stents (available from Guidant Corporation) were coated using embodiments of the method of the present invention. The stents were cleaned by sonication in water, followed by sonication in isopropanol. The stents were dried at 70°C and plasma cleaned in an argon plasma chamber.

[0041] Each unexpanded stent was positioned on a mandrel such that the mandrel contacted the stent at its opposing ends. An EFD 780S spray device with VALVEMATE 7040 control system (manufactured by EFD Inc., East Providence, RI) was used to apply the coating compositions to the stents. The spray nozzle was adjusted to provide a distance from the nozzle tip to the outer surface of the stent of

approximately 4.5 cm and a spray angle of approximately 90° relative to the horizontal stents. The atomization pressure was set to be maintained throughout the coating process at 20 psi.

[0042] Each stent was passed under the spray nozzle for about 2 seconds. A composition containing 2% (w/w) poly-n-butyl methacrylate (PBMA) 337K in cyclohexanone:ethyl acetate (1:1) was sprayed onto one stent. A composition containing 2% (w/w) PBMA 649K in cyclohexanone:ethyl acetate (1:1) was sprayed onto two stents. A composition containing 2% (w/w) PBMA 857K in cyclohexanone:ethyl acetate (1:1) was sprayed onto one stent. Each stent was rotated about the stent's central longitudinal axis at a speed of 3 rpm during coating. After a waiting period of 1 second following the application of the respective compositions, warm air of approximately 80°C was directed from an air gun onto each stent for 15 seconds to remove most of the solvents. The spraying-blowing cycle was repeated to deposit thirty-four layers on each stent, with a wait time of 5 seconds between each cycle. The coated stent was allowed to dry for about 60 minutes under vacuum conditions in an oven at a temperature of about 70°C.

[0043] Each of the four coated stents had a uniform, smooth coating. In addition, the stent sprayed with 2% (w/w) PBMA 857K in cyclohexanone:ethyl acetate (1:1) was submitted for a simulated use test and was found to have good mechanical properties, no cracking, and good coating adhesion.

Example 2

[0044] An 8 mm Multi-Link TETRA stent was coated using embodiments of the method of the present invention. The stent was cleaned by placement in an ultrasonic bath of isopropyl alcohol solution for 15 minutes. The stent was dried and plasma cleaned in a plasma chamber.

[0045] A composition containing 2% (w/w) poly-n-butyl methacrylate (PBMA) and 2% (w/w) quinoline yellow dye in chloroform:cyclohexanone (9:1) was prepared.

[0046] The unexpanded stent was positioned on a mandrel such that the mandrel contacted the stent at its opposing ends. An EFD 780S spray device with VALVEMATE 7040 control system was used to apply the coating composition to the stent. The spray nozzle was adjusted to provide a distance from the nozzle tip to the outer surface of the stent of 1.25 inches (3.18 cm) and a spray angle of approximately 90° relative to the horizontal stent. The atomization pressure was set to be maintained throughout the coating process at 15 psi.

[0047] The stent was passed under the spray nozzle for about 1 second. The stent was rotated about the stent's central longitudinal axis at a speed of 3 rpm during coating. Warm air of approximately 100°C was directed from an air gun onto the stent for 4 seconds to remove most of the solvents. The spraying-heating cycle was repeated to deposit forty layers on the stent, depositing about 300 micrograms of coating. The coated stent was allowed to dry for about 3 hours under vacuum

conditions at a temperature of about 75°C. The coated stent had a uniform, smooth coating with an estimated dye content of about 130 micrograms or 43% of the total amount of coating deposited.

Example 3

[0048] An 8 mm Multi-Link TETRA stent was coated using embodiments of the method of the present invention. The stent was cleaned by placement in an ultrasonic bath of isopropyl alcohol solution for 15 minutes. The stent was dried and plasma cleaned in a plasma chamber.

[0049] A primer composition containing 2% (w/w) poly-n-butyl methacrylate (PBMA) was prepared. A reservoir composition containing 2% (w/w) PBMA and 2.7% (w/w) ethyl eosin dye in methanol:cyclohexanone (1:1) was also prepared. In addition, a diffusion barrier composition containing 2% (w/w) PBMA was prepared.

[0050] The unexpanded stent was positioned on a mandrel such that the mandrel contacted the stent at its opposing ends. An EFD 780S spray device with VALVEMATE 7040 control system was used to apply the various compositions to the stent. The spray nozzle was adjusted to provide a distance from the nozzle tip to the outer surface of the stent of 1.25 inches (3.18 cm) and a spray angle of approximately 90° relative to the horizontal stent. The atomization pressure was set to be maintained throughout the coating process at 15 psi. The stent was rotated about the stent's central longitudinal axis at a speed of 3 rpm during coating.

[0051] The primer composition was applied to the stent by passing the stent under the spray nozzle for about 0.75 second. Warm air of approximately 100°C was directed from an air gun onto the stent for 8 seconds to remove most of the solvents and form a primer layer on the stent. The reservoir composition was then applied to the primered stent by passing the stent under the spray nozzle for about 0.75 second. Warm air of approximately 100°C was directed from an air gun onto the stent for 4 seconds to remove most of the solvents. The spraying-heating cycle was repeated to deposit forty layers on the stent, depositing about 419 micrograms of the reservoir coating. The coated stent was allowed to dry for about 3 hours under vacuum conditions at a temperature of about 75°C. The barrier layer composition was then applied to the reservoir-coated stent by passing the stent under the spray nozzle for about 0.75 second. Warm air of approximately 100°C was directed from an air gun onto the stent for 4 seconds to remove most of the solvents. The spraying-heating cycle was repeated to deposit about 70 micrograms of the diffusion barrier. The coated stent was allowed to dry overnight under vacuum conditions at a temperature of about 75°C. The coated stent had a uniform, smooth coating with an estimated dye content of about 224 micrograms or 53% of the total amount of coating deposited.

Example 4

[0052] An 8 mm Multi-Link TETRA stent was coated using embodiments of the method of the present invention. The stent was cleaned by placement in an ultrasonic

bath of isopropyl alcohol solution for 15 minutes. The stent was dried and plasma cleaned in a plasma chamber.

[0053] A composition containing 2% (w/w) poly-n-butyl methacrylate (PBMA) and 2% (w/w) quinoline yellow dye in chloroform:cyclohexanone (9:1) was prepared.

[0054] The unexpanded stent was positioned on a mandrel such that the mandrel contacted the stent at its opposing ends. An EFD 780S spray device with VALVEMATE 7040 control system was used to apply the composition to the stent. The spray nozzle was adjusted to provide a distance from the nozzle tip to the outer surface of the stent of 1.25 inches (3.18 cm) and a spray angle of approximately 90° relative to the horizontal stent. The atomization pressure was set to be maintained throughout the coating process at 15 psi.

[0055] The stent was passed under the spray nozzle for about 1.5 second. The stent was rotated about the stent's central longitudinal axis at a speed of 3 rpm during coating. Warm air of approximately 100°C was directed from an air gun onto the stent for 4 seconds to remove most of the solvents. The spraying-heating cycle was repeated to deposit 3 layers on the stent, depositing about 115 micrograms of coating. The coated stent was allowed to dry for about 3 hours under vacuum conditions at a temperature of about 75°C. The coated stent had a uniform, smooth coating with an estimated dye content of about 38 micrograms or 33% of the total amount of coating deposited.

Example 5

[0056] To determine the maximum amount of coating that could be deposited on an 8 mm stent without visible webbing, a Multi-Link TETRA stent was coated using the same coating composition and parameters as described in Example 4. The spraying-heating cycle was repeated until 790 micrograms of coating had been deposited on the stent, at which time no webbing was observed.

Example 6

[0057] An 8 mm Multi-Link TETRA stent was coated using embodiments of the method of the present invention. The stent was cleaned by placement in an ultrasonic bath of isopropyl alcohol solution for 15 minutes. The stent was dried and plasma cleaned in a plasma chamber.

[0058] A composition containing 2% (w/w) poly-n-butyl methacrylate (PBMA) and 2% (w/w) solvent blue dye in chloroform:cyclohexanone (9:1) was prepared.

[0059] The unexpanded stent was positioned on a mandrel such that the mandrel contacted the stent at its opposing ends. An EFD 780S spray device with VALVEMATE 7040 control system was used to apply the composition to the stent. The spray nozzle was adjusted to provide a distance from the nozzle tip to the outer surface of the stent of 1.25 inches (3.18 cm) and a spray angle of approximately 90° relative to the horizontal stent. The atomization pressure was set to be maintained throughout the coating process at 15 psi.

[0060] The stent was passed under the spray nozzle for about 1.5 seconds. The stent was rotated about the stent's central longitudinal axis at a speed of 3 rpm during coating. Warm air of approximately 100°C was directed from an air gun onto the stent for 4 seconds to remove most of the solvents. The spraying-heating cycle was repeated to deposit about 130 micrograms of coating. The coated stent was allowed to dry for about 3 hours under vacuum conditions at a temperature of about 75°C. The coated stent had a uniform, smooth coating with a estimated dye content of about 85 micrograms or 66% of the total amount of coating deposited.

[0061] While particular embodiments of the present invention have been shown and described, it will be obvious to those skilled in the art that changes and modifications can be made without departing from this invention in its broader aspects. Therefore, the appended claims are to encompass within their scope all such changes and modifications as fall within the true spirit and scope of this invention.